ALKYLATION OF SOME TRICARBONYL(PENTADIENYL) AND (CYCLOHEXADIENYL)IRON(+1) SALTS WITH THE HIGHLY FUNCTIONALIZED COPPER REAGENTS RCu(CN)ZnI

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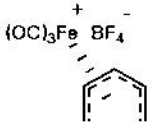
Summary: Reaction of the highly functionalized copper reagents RCu(CN)ZnI with the title compounds occurs predominantly at less hindered termini, generating functionalized side chains at C5 of (η^4-penta-1,3-diene) and (η^4-clohexa-1,3-diene)tricarbonyliron(0) complexes.

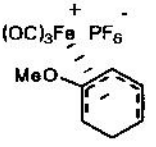
The addition of carbon nucleophiles to (η^5-pentadienyl) and (η^5-cyclohexadienyl)tricarbonyliron(+1) salts offers an easy access to a variety of the C5 substituted (η^4-penta-1,3-diene) and (η^4-clohexa-1,3-diene)-tricarbonyliron(0) complexes. The applications of the resulting complexes to the synthesis of natural products are well documented.[2] Several classes of stablized lithium nucleophiles such as enolates,[3] as well as nonstabilized lithium,[4] magnesium,[5] cadmium,[6] and zinc[6] organometallics have been shown to add to the cations (**1-4**). However, there are some disadvantages among these alkylating reagents. Reaction of the cation (**1**) with lithium reagents occurred at both C2 and C1 positions of the π-system, generating a mixture of σ,η^3-iron complexes and η^4-diene complexes.[4a] Reaction of the cation (**2**) with dimethyl sodiomalonate proceeded by attacking at both C1 and C5 termini (C1/C5=1/1.8) in only 51% yield.[7] Reaction of Grignard reagents with the cation **3** has been shown to lead by reductive coupling to the bis 5,5' (η^4-cyclohexa-1,3-diene)tricarbonyliron(0) complex or to decomposition.[5] Organo-cadmium and -zinc reagents (prepared in ether or THF by reaction of the appropriate Grignard reagents with cadmium and zinc chloride) reacted with cations (**3**) or (**4**) to give adducts only in satisfactory yields.[3] Moreover, the alkylation is unsuccessful with dimethylzinc and dimethylcadmium. Surprisingly, the reports on the addition of organocuprates to cations (**1-4**) are rare.[8] Furthermore, organocuprates obtained from the corresponding lithium reagents and copper salts do not bear functional groups. Recently Knochel has found that polyfunctionalized copper reagents can be generated by transmetallation of the corresponding functionalized zinc compounds with CuCN.2LiCl in THF.[9] We now report a general preparation of (η^4-1,3-diene)tricarbonyliron(0) derivatives (**6a-6l**) with functionalized side chains at C5 by reaction of the functionalized copper reagents with cations (**1-4**).[10] The reaction are performed in the expection that further manipulation of the molecules will then be possible after the intial additions.



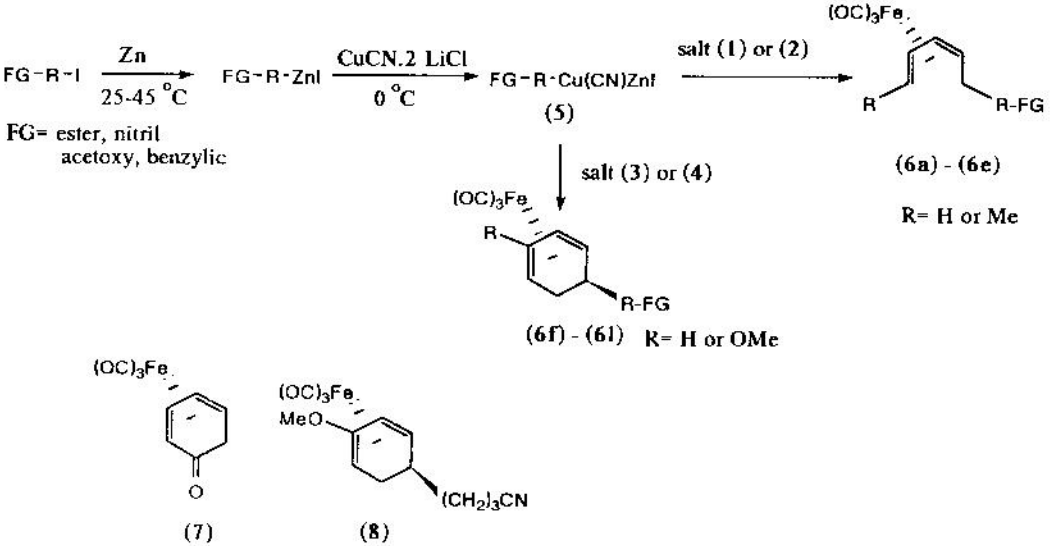
(**1**)

(**2**)

(**3**)



(**4**)

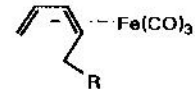
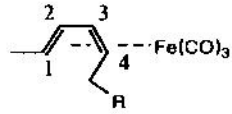
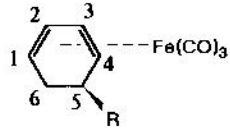
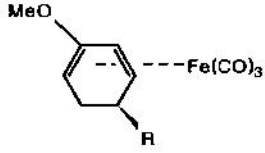


Excess functionalized copper reagents (1.6 mol-eq) is added at 5 °C under nitrogen to a stirred suspension of the cations (**1-4**) in dry THF. The reaction mixture is stirred at 28 °C for 2h.[11] The yields of the addition are generally high (60-98%, Table) after chromatographed on silica gel. The highly reactive benzylic copper reagent (**5d**) adds smoothly under our reaction conditions to give complexes (**6d**), (**6i**), and (**6k**) (see Entries 4, 9, and 11, Table) with higher yields than the benzylic zinc compound.[6a] However, with the less reactive cation (**4**),[4b] the reactions became very sluggish with copper reagents (**5a**) and (**5b**). Addition of the copper reagent (**5b**) to the cation (**4**) did not give the desired adduct. Instead, (η^4-cyclohexa-2,4-diene-1-one)tricarbonyliron(0) complex (**7**) was isolated in 70% yield after hydrolysis of the reaction mixture.[12] While the addition of the copper reagent (**5a**) to the cation (**4**) gave the desired adduct (**8**) in only 45% yield together with a significant ammount of complex (**7**). The addition is highly regioselective (C5 attack) with cations (**2**) and (**4**). Normally less than 5% of C1 adducts can be detected in the crude reaction mixture by 200 MHz ^{1}H NMR spectroscopy. The results are consistent with organocuprates attacking at less sterically hindered sites.[8] The stereochemistry assignment for diene complexes (**6a**), (**6b**), (**6c**) (Z), and (**6d**), (**6e**) (E, Z) is based on the coupling constants of the adjacent protons. For instance, the ^{1}H NMR spectroscopic data of complex (**6e**) exhibits a signal at δ 5.22 (dd, J= 5.0, 9.0 Hz) for H2 and a signal at δ 5.09 (dd, J= 5.0, 7.0 Hz) for H3 (see Entry 5, Table).[8b] The easy available of the (η^4-1,3-diene)tricarbonyliron(0) complexes with functionalized side chains at C5 might be used as convienient precursors for natural products synthesis. For example, introduction of a 3-propylnitrile group to a (η^4-cyclohexa-1,3-diene)tricarbonyliron(0) derivative took 5 steps starting with dimethyl potassiomalonate and the cations in 29% overall yield.[12] While under our reaction conditions, complex (**6g**) is obtained in only one step and 78% yield.

In conclusion, we have demonstrated that (η^4-penta-1,3-diene) and (η^5-cyclohexa-1,3-diene)-tricarbonyliron(0) complexes with various functionalized side chains at C5 are accessible by the reaction of the functionalized copper reagents with (η^5-pentadienyl) and (η^4-cyclohexadienyl)tricarbonyliron(+1) salts. Further extensions and synthetic applications of these studies are currently under way in our laboratory.

Acknowledgement . This research was supported financially by a grant from the National Science Council ROC (NSC80-0208-M003-18) and Department of Chemistry, Academia Sinica.

Table. (η^4-Diene)tricarbonyliron(0) Complexes (**6a-6l**) Obtained by the Addition of the Functionalized Copper Reagents (**5a-5d**) to the Cationic Salts (**1-4**)

Entry	FG-RCu(CN)ZnI	Cationic Salt	Product	Yield(%)[a]
1	$NC(CH_2)_3Cu(CN)ZnI$ (**5a**)	(**1**)		
			(**6a**) : R= $NC(CH_2)_3$-	90
2	$NC(CH_2)_2Cu(CN)ZnI$ (**5b**)	(**1**)	(**6b**) : R= $NC(CH_2)_2$-	84
3	$EtO_2C(CH_2)_3Cu(CN)ZnI$ (**5c**)	(**1**)	(**6c**) : R= $EtO_2C(CH_2)_3$-	97
4	$PhCH_2Cu(CN)ZnBr$ (**5d**)	(**2**)		
			(**6d**) : R= Ph_2CH_2-	96
5	(**5a**)	(**2**)	(**6e**) : R= $NC(CH_2)_3$-	98
6	(**5a**)	(**3**)		
			(**6f**) : R= $NC(CH_2)_3$-	75
7	(**5b**)	(**3**)	(**6g**) : R= $NC(CH_2)_2$-	78
8	(**5c**)	(**3**)	(**6h**) : R= $EtO_2C(CH_2)_3$-	83
9	(**5d**)	(**3**)	(**6i**) : R= $PhCH_2$-	81
10	$AcO(CH_2)_4Cu(CN)ZnI$ (**5e**)	(**3**)	(**6j**) : R= $AcO(CH_2)_4$-	60
11	(**5d**)	(**4**)		
			(**6k**) : R= $PhCH_2$-	92
12	(**5c**)	(**4**)	(**6l**) : R= $EtO_2C(CH_2)_3$-	76

[a]All products described in this table are purified and exhibit spectral (^{1}H NMR, ^{13}C NMR, IR, Mass) and analytical (HRMS) data consistent with the assigned structures.

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10. For cations (1) and (2), see Mahler, J. E.; Gibson, D. H.; Pettit, R. *J. Am. Chem. Soc.* **1963**, 85, 3959. For cations (3) and (4), see Pearson, A. J. *J. Chem. Soc. Perkin I* **1980**, 2239.
11. A typical experimental procedure follows: A solution of functionalized cooper reagents (5c) (8 mmol, prepared from 4-iodo ethylbutyrate and zinc, followed by transmetallation with CuCN.2LiCl) in THF (10 ml) was added at 5 °C under nitrogen to a stirred suspension of the cation (3) (1.90 g, 5 mmol) in THF (5 ml). After stirring (2h) at 23 °C, a homogeneous solution was obtained. The resulting mixture was quenched with saturated aqueous ammonium chloride solution (5 ml). The reaction mixture was then extracted with ether (50 ml), washed 3x with water (40 ml), and 3x with brine (40 ml). The organic layer was dried over sodium sulfate, filtered and the solvent removed under reduced pressure. The residue (2.0 g) was chromatographed on silica gel (100 g) using hexane : ethyl acetate (20:1) as eluent. The yellow fraction was concentrated and distilled under *vacuo* (140 °C, 0.5 mmHg) to give the adduct (6h) as a yellow oil (1.38 g, 3.98 mmol, 83%). (6h): Characteristic IR peak (neat): 2043, 1964, 1743 cm^{-1}. ^1H NMR ($CDCl_3$, 200 MHz): δ 5.32 (m, 1 H, H2 or H3), 5.23 (m, 1 H, H2 or H3), 4.07 (q, J=7.2 Hz, 2 H, CO_2CH_2-), 3.08 (m, 1 H, H1 or H4), 3.00 (m, 1 H, H1 or H4), 2.19 (t, J= 7.3 Hz, 2 H, CH_2CO_2-), 2.00-1.88 (m, 2 H, H1 and endo H6), 1.51 (m, 2 H, CH_2-C-C-CO_2-), 1.17 (t, J=7.1, Hz, 3 H, CO_2-C-CH_3), 1.28-1.05 (m, 3 H, exo H6 and CH_2-C-CO_2-). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 212.08, 173.39, 85.52, 84.47, 66.53, 60.15, 59.79, 39.32, 37.86, 34.22, 30.63, 23.50, 14.17. Mass (EI) : 334 (M^+, 3), 306 (M- CO, 7), 278 (M-2 CO, 45), 250 (M-3 CO, 100).
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(Received in Japan 21 September 1990)